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## Quercetin: A Promising Bioflavonoid for Health and Healing Md Shariful Islam<sup>\*1</sup>, Sruti Karmakar<sup>2</sup>

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#### Abstract:

Quercetin, a vital natural polyphenolic flavonoid, has diverse pharmacological activities and therapeutic potential. Flavonoids have emerged as a fundamental component in various cosmetic, pharmaceutical, and medicinal formulations. Quercetin is widely recognized for its numerous health benefits, encompassing antioxidant, anti-inflammatory, antiviral, and anticancer properties and due to its wide spectrum of health-promoting effects, quercetin has attracted much attention from dietitians and medicinal chemists. Despite its promising benefits, quercetin faces challenges such as poor solubility, limited water solubility, chemical instability, and low oral bioavailability significantly restrict its potential applications. Strategies such as formulation optimization and nanoparticle-based delivery systems are being explored to enhance its pharmacokinetic profile. Understanding the pharmacology, biochemistry, and pharmacokinetics of quercetin is crucial for optimizing its therapeutic potential and designing precise drug for clinical use. Further scientific research is necessary to elucidate its mechanisms and enhance clinical utilization.

#### **Introduction:**

Since ancient times, plants have played a crucial role in the treatment of infectious diseases. In recent years, the popularity of natural products has surged both in developing and developed nations, leading to the widespread availability of herbal medicines not only in drug stores but also in supermarkets and food stores. Additionally, extensive research has explored the biological and pharmacological activities of various phytoconstituents and chemical compounds extracted from medicinal herbs (Sarkar et al., 2016; Bansal and Priyadarsini, 2021; Das et al., 2022; Pawar et al., 2023). Through isolating and characterizing these phytochemicals, the scientists aim to explain their mechanisms of action, pharmaco-kinetics and possible applications in the treatment of different diseases (Acharya et al., 2022a; 2022b; Ghosh et al., 2022). The activities thus not only enrich our knowledge of traditional herbal remedies but also, at the same time, create a way in which the development of new pharmaceuticals with better efficacy and fewer side effects will take place, thus bridging the gap between traditional wisdom and modern medicine (Maiti et al., 2010, 2013; Banerjee et al.,

#### Md. Shariful Islam\*

Department of Zoology, Jhargram Raj College, Jhargram, West Bengal, India E-mail: shariful.zoology@gmail.com; Orcid iD: https://orcid.org/0009-0003-8457-4537 **Sruti Karmakar** Department of Environmental Science, Asutosh College, Kolkata, West Bengal, India E-mail: sruti.karmakar@asutoshcollege.in; Orcid iD: https://orcid.org/0000-0002-5502-1330 \***Corresponding Author**: shariful.zoology@gmail.com

© International Academic Publishing House, 2023 Mrs. Bhanumati Sarkar, Dr. (Professor) Surjyo Jyoti Biswas, Dr. Alok Chandra Samal & Dr. Akhil Pandey (eds.), The Basic Handbook of Indian Ethnobotany and Traditional Medicine [Volume: 2]. ISBN: 978-81-962683-5-0; pp. 117-134; Published online: 15th December, 2023 2014; Sarkar et al., 2021). Among these compounds, Quercetin (Qct), a polyphenolic flavonoid, has garnered significant attention due to its diverse pharmacological activities, which include antioxidant, antiviral, immune-modulatory, and anticancer properties, coupled with a low toxicity profile. Chemically composed of three benzene rings and five hydroxyl groups, Qct (3,5,7,3',4'-pentahydroxyflavone) is the principal polyphenolic flavonoid found in a variety of vegetables and fruits, such as berries, lovage, capers, cilantro, dill, apples, and onions, as well as in flowers, bark, stems, and roots, and even in wine (Aghababaei et al., 2023). This book chapter aims to explore the pharmacological effects of Qct, its clinical applications, and important safety considerations

# Structure, bioavailability, dose, metabolism and excretion of Qct Structure

Qct, presents a yellow hue and demonstrates high solubility in lipids and alcohol. However, it exhibits limited solubility in cold water and remains insoluble in hot water. The name "Quercetin" finds its roots in the Latin term "Quercetum," which denotes Oak Forest. Belonging to the flavonol category, Quercetin is not naturally produced within the human body. According to the International Union of Pure and Applied Chemistry (IUPAC) nomenclature, Quercetin is designated as 2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxychromen-4-one, with a chemical formula represented by C<sub>15</sub>H<sub>10</sub>O<sub>7</sub>. Quercetin, categorized as a flavonol flavonoid, exhibits a molecular structure typical of polyphenolic compounds. With its chemical composition of C<sub>15</sub>H<sub>10</sub>O<sub>7</sub>, it comprises two benzene rings (A and B) connected to a heterocyclic pyrene (C). A notable feature of Quercetin is the presence of five hydroxyl groups (OH) situated at positions 3, 5, 7, 3', and 4'. These hydroxyl groups exert a significant influence on the biological activities of the compound and contribute to the potential diversity of derivative compounds that can be synthesized from it.

Qct exhibits a wide range of pharmacological activities, including anticancer, antiviral, antiallergic, metabolic, and anti-inflammatory effects. It also shows promise in treating eye and cardiovascular diseases, as well as arthritis. Additionally, Qct has demonstrated potential as a cancer-preventive agent and possesses psychostimulant properties. It notably inhibits platelet aggregation, reduces capillary permeability, mitigates lipid peroxidation, and enhances mitochondrial biogenesis.

#### **Bioavailability**

Bioavailability refers to the proportion of a chemical that effectively reaches its intended site of action. Qct is initially consumed in the form of glycosides, with glycosyl groups being liberated during mastication, digestion, and absorption. Subsequently, Qct glycosides undergo conversion into aglycone within the intestine, facilitated by the action of  $\beta$ -glycosidase enzymes, before being absorbed into enterocytes. However, various factors such as poor water solubility, extensive hepatic and intestinal epithelial metabolism leading to the formation of metabolites with reduced biological activity, and interactions with the intestinal microbiota can significantly impact the absorption and metabolism of Qct (Degroote et al., 2019).

Given its lipophilic nature, Qct can traverse intestinal membranes via simple diffusion. It is generally presumed that absorption is more efficient in its aglycone form compared to its glycosidic counterparts, which may reach the intestines without degradation (Nemeth et al., 2007). Studies involving patients with ileostomies have indicated a higher absorption rate of Qct glycosides from onions compared to the pure aglycone form (Hollman et al., 1995). Furthermore, research aimed at identifying food sources that optimize Qct absorption has demonstrated that Qct present in onions exhibits superior absorption compared to that in tea (De Vries et al., 1998).

On the contrary, Scholz and Williamson have documented significant levels of aglycone in ileostomy fluid samples obtained from patients who had consumed meals containing onions. Interestingly, they noted a high concentration of Qct glycosides alongside a minor presence of Qct aglycone, with the absence of Qct glycosides in the fluid. One plausible explanation is the enzymatic hydrolysis of Qct glycosides, facilitated by  $\beta$ -glycosidase enzymes, leading to the formation of aglycone. These enzymes are predominantly located in the small intestine, where they catalyze this conversion, after which most of them are absorbed.

#### Daily recommended dose of Qct

It has been estimated that daily Qct intake typically falls within the range of 5 to 100 mg, primarily based on fruit and vegetable consumption. However, heavy consumption of Qct-rich foods can elevate daily intake to as high as 500 mg (Harwood et al., 2007; Bischoff et al., 2008; Russo et al., 2012). Studies have revealed that the effectiveness of the dose increases notably when Qct is consumed alongside a fatty meal or in conjunction with apple pectin, oligosaccharides, and lecithin (Harwood et al., 2007; Russo et al., 2012). In clinical settings, Qct is commonly administered at doses ranging from 500 to 1000 mg per day, divided into multiple doses (Lee et al., 2012; Edwards et al., 2007). Research shows that when Qct is taken as a dietary supplement, there is a significant increase in serum levels, although the extent of this increase varies greatly among individuals (Kressler et al., 2011).

### Metabolism and excretion of Qct

Immediately after absorption, Qct is transported to the liver, where it undergoes metabolism and the derived metabolites subsequently enter the bloodstream for distribution throughout the body's tissues (Hollman, 2004). Mullen et al. (2006) identified the primary metabolites of Qct in plasma as Qct-3-O-sulfate, Qct-3-O-glucuronide, and Qct-3-O-sulfate, while Qct-3-O-glucuronide, Qct diglucuronide, isorhamnetin-O-glucuronide-sulfate, isorhamnetin-methyl-Qct, and diglucuronideisorhamnetin-glucuronide were detected in urine samples from healthy individuals following onion ingestion.

The short half-life and rapid clearance of Qct metabolites from the bloodstream result in their rapid detection in plasma within just 30 minutes of ingestion, with substantial excretion

occurring over a 24-hour period (Moon et al., 2008). Moon et al. (2000) also indicated the aggregation of Qct conjugates in human plasma following repeated consumption of Qct-rich foods.

## **Biological activities of Qct Neuroprotective effect:**

Qct increases toxicity-induced neuronal cell damage and stabilizes intracellular calcium concentration. It has been found that an unnecessary increase in intracellular calcium causes neuronal cell death, which in turn leads to ischemic stroke. It is demonstrated that the calciumbinding protein is modulated to reduce calcium excess in Qct's neuroprotective activity against cerebral ischemia (Park et al., 2020). It has been reported that a number of metabolic syndromes linked to prenatal and early postnatal stress are diminished with treatment by Qct and kaempferol. Qct and kaempferol modulate leptin and ghrelin levels along with antioxidant pathways to prevent alterations in metabolism and brain functioning brought on by prenatal and early postnatal dietary shortages (Anachuna et al., 2020). Oxidative stress, mitochondrial dysfunction, neuroinflammation, and apoptosis associated with neurodegenerative diseases (Alzheimer's, Parkinson's, Huntington's diseases) have been shown to be affected by Qct. Studies conducted on rat models with intracerebral hemorrhage, transgenic mouse models of Alzheimer's Disease (AD), and streptozotocin-induced diabetic rat models have found that Qct improves neurological abnormalities. Qct has been advertised as having the ability to reduce oxidative stress and neurotoxicity when administered in vivo along with a variety of metals, pesticides, and neurotoxins. It is also proven that Qct exposure alone has negative effects on fish (Channa punctata), although it has protective effects on fish with oxidative stress (Wu et al., 2021)

#### **Cardioprotective effect:**

Studies indicate that hypoxic environments are responsible for oxidative stress, leading to the loss of heart function as cardiomyocytes undergo apoptosis. An effective preventive or therapeutic approach for CVD is to halt the progression of apoptosis due to the critical role that cardiomyocyte loss plays in morbidity and death (Guo et al., 2019). Qct has been found to be a wonderful potential cardioprotective agent. Its antioxidative and antiplatelet properties significantly impact muscle function. These properties include inhibiting smooth muscle cell migration and proliferation, improving mitochondrial function of cardiac cells, and inhibiting nuclear factor-kappa light chain-enhancer of activated B cells (NF-B) (64). Qct is believed to regulate blood pressure by affecting the renin-angiotensin-aldosterone system (RAAS) and enhancing vascular function. A significant antihypertensive effect has been revealed as Qct is taken by people with hypertension or prehypertension at doses of 500 mg/day and above. Qct has also been found to improve vascular function by increasing the bioavailability of nitric oxide produced in endothelial cells. Several studies show that it lowers blood triglyceride levels while affecting no other plasma lipids. Qct plays a pivotal role in Atherosclerosis (AS) and Atherosclerotic Cardiovascular Disease (ASCVD), chronic inflammatory diseases characterized by endothelial dysfunction, abnormalities in lipid metabolism, and oxidative stress (Deng et al., 2020). Qct's anti-inflammatory effects can reduce cardiovascular risk factors such as fibrinogen and C-reactive protein (Bhat et al., 2021). With its anti-inflammatory, antioxidative, regulation of lipid metabolism abnormalities, and other properties, Qct inhibits AS plaque formation in the treatment of ASCVD.

Recent research establishes a potential association between depression and cardiovascular illness and brain-derived neurotrophic factor (BDNF). Qct is known to reduce behavioral dysfunction by lowering hippocampus oxidative stress (Wang et al., 2021). Besides its cardiovascular effects, Qct also provides strong protection against various cardiac injuries, such as ischemia-reperfusion (I/R) injury, doxorubicin-induced cardiotoxicity, diabetic cardiomyopathy, and others, by regulating a variety of signaling pathways and proteins. It acts by decreasing oxidative stress and inhibiting apoptosis, as well as affecting inflammatory proteins in the heart (Ferenczyova et al., 2020).

## **Osteoprotective effect**

Having strong osteo-inductive and angiogenic properties, Qct and its derivatives might support the differentiation of bone marrow stem cells (BMSCs) into osteoblasts (Ren et al., 2022). Studies have shown Qct's positive interactions with bone cells, promoting osteoblast growth while slowing or halting osteoclast activity. Research has also indicated Qct's critical role in regulating bone tissue renewal and inflammation (Huang et al., 2021). It has been demonstrated that both Qct and kaempferol significantly enhance bone mineralization, bone microstructure, and osteoblast activity in estrogen deficiency-induced bone loss and ovariectomized rats (Wong et al., 2020). A significant increase in the levels of tumor necrosis factor-alpha (TNF-a), heightened oxidative stress, interleukin (IL)-6, and IL-1beta impact bone metabolism. Additionally, osteoclast differentiation and bone resorption occur via reactive oxygen species (ROS), while oxidative stress and inflammatory cytokines stimulate osteoclast development. Osteoclasts, specialized bone-resorbing cells, are regulated by nuclear factor kappa-B ligand and macrophage colony-stimulating factor (M-CSF) (RANKL). Qct plays a crucial role in treating Rheumatoid Arthritis (RA), a chronic inflammatory disease characterized by synovial inflammation and joint destruction. Thus, it can be inferred that Qct controls osteoclast genesis in RA in various ways, including reducing the level of RANKL in RAFLS, inhibiting osteoclast differentiation of monocytes from RANKL and IL-17, and regulating the development of Th17 cells (Anachuna et al., 2020).

## **Antioxidant activity**

Qct is widely known as a potent natural flavonoid with antioxidant properties that protect our body from free radicals by reducing or inhibiting damage and oxidative stress in both in vitro and in vivo studies. According to Lesjak et al. (2018), Qct-derived metabolites (e.g., isorhamnetin and tamarixetin) showed higher antioxidant activity than Qct by inhibiting lipid peroxidation. In vivo studies indicated antioxidant and hepatoprotective effects against acute liver damage induced by tertiary butyl hydrogen peroxide. Qct has also been found to have a protective function against radiation-induced damage and genetic toxicity (Kalantari et al., 2018).

Age-related macular degeneration (AMD) is characterized by vision loss in older people. Reactive oxygen intermediates are responsible for damaging retinal pigment epithelial cells (RPEs). With its cytoprotective property, Qct is considered a good agent in reducing the risk of developing AMD. Several studies have also demonstrated the role of Qct in inhibiting oxidative stress-mediated neuronal damage. Its radical-scavenging and metal-chelating activities reduce a number of neurodegenerative disorders and vascular pathologies in the brain.

#### **Anti-inflammatory activity**

Quercetin exhibits potent anti-inflammatory effects and has a long half-life. In a mouse model, where Qct and galangin were administered either alone or in combination, both substances were found to reduce interleukin-6 (IL-6), NF-kB, and nitric oxide production in lipopolysaccharide (LPS)-stimulated RAW264.7 macrophages. Additionally, histological analysis and measurements of ear thickness revealed a significant reduction in IgE levels and inflammation. This suggests that the combination of Qct and galangin offers novel strategies for preventing atopic dermatitis (AD) (Lee, H.N. et al; 2018).

In various in vitro studies, Qct has been shown to inhibit the growth of IL-8-induced LPS in lung A549 cells and the production of lipopolysaccharide (LPS)-mediated tumor necrosis factor (TNF- $\alpha$ ) in macrophages. Furthermore, Qct can decrease the amounts of TNF- $\alpha$  and interleukin (IL)-1 $\alpha$  produced by LPS, thus reducing apoptotic neuronal cell death driven by activated microglia (Saeedi-Boroujeni et al.,2021). Studies have demonstrated that Qct effectively inhibits the NLRP3 inflammasome, which activates multiple inflammatory mediators, including NRF2, TXNIP, and SIRT1. This suggests that Qct may be a potential therapy for severe inflammation, such as that seen in COVID-19 (Saeedi-Boroujeni et al.,2021).

In peripheral blood mononuclear cells (PBMC) under normal conditions, Qct significantly upregulates the gene expression and production of interferon- $\gamma$  (IFN- $\gamma$ ) from T helper cell 1 (Th1) and downregulates IL-4 from Th2. Additionally, Qct is known to decrease the production of inflammatory molecules such as COX-2, nuclear factor-kappa B (NF- $\kappa$ B), activator protein 1 (AP-1), mitogen-activated protein kinase (MAPK), reactive nitric oxide synthase (NOS), and reactive C-protein (CRP) (Lee, H.N. et al; 2018).

#### **Anti-diabetic activity**

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by increased cellular resistance to insulin or a deficiency in insulin secretion, leading to disturbances in protein, carbohydrate, and lipid metabolism (Poznyak et al., 2020; Sarkar et al., 2023). Several studies have suggested that Qct shows anti-diabetic properties by promoting insulin secretion and

modulating carbohydrate metabolic enzymes (Sur et al., 2023; Biswas et al., 2023; Roy et al., 2023; Acharya et al., 2023). Research indicates that Qct may play a protective role against streptozotocin (STZ)-induced toxicity, alleviating oxidative stress in the pancreas and promoting insulin secretion, thereby restoring pancreatic islet function in STZ-induced diabetes (Jaishree et al., 2020). Hemmati et al. (2018) investigated the effect of Qct as a dietary supplement and found it to be critical in regulating the expression of key enzymes involved in glucose metabolism, including glucokinase and glucose-6-phosphatase. Additionally, Qct has been shown to mitigate gestational diabetes by modulating adiponectin signaling and its receptors, thereby restoring the expression of these enzymes (Mahabadi et al., 2021). Furthermore, studies have demonstrated that Qct exerts significant inhibitory effects on the activities of alpha-amylase and alpha-glucosidase in a concentration-dependent manner, while also protecting against lipid oxidation in pancreatic tissue homogenates (Oboh et al., 2015). Higher Qct consumption has been associated with a reduced risk of type 2 diabetes mellitus (T2DM) in the Chinese adult population (Yao et al., 2019). In the context of diabetic osteopenia, Qct has been shown to play a role in rebuilding bone architecture damaged by diabetes (Hemmati et al., 2018). Moreover, Qct has been found to prevent the increase in acetylcholinesterase (AChE) activity induced by diabetes in the cerebral cortex and hippocampus. Additionally, it reduces cholinergic signaling and aids in the restoration of lost memory in diabetic rats by enhancing acetylcholine (ACh) function (Maciel et al., 2016).



Figure 1. Diverse biological role and therapeutic applications of quercetin, a potent flavonoid found in various plant-based foods. From antioxidant and anti-inflammatory properties to potential benefits in cardiovascular health, and cancer prevention, quercetin emerges as a versatile molecule with promising implications for human health and disease management.

#### Anti-hyperuricemic activity

Recently, hyperuricemia has gained increased attention among people not only because of its primary association with gout but also due to its significant threat in developing associated illnesses such as cardiovascular disease (CVD) and chronic kidney disease (CKD). Essentially, hyperuricemia denotes an elevated level of serum urate, resulting in the accumulation of monosodium urate crystals in joint tissue interstitial spaces, leading to gout (Tumova et al., 2021).Qct plays a significant role in preventing hyperuricemia by inhibiting a number of enzymes related to urate production, supporting the activity of urate excretion transporters, and controlling the activity of urate reabsorption transporters. Additionally, it reduces the risk of hyperuricemia by enhancing the antioxidant defense system to remove free radicals and by mitigating comorbid conditions associated with gout and hyperuricemia, such as hypertension, diabetes, obesity, dyslipidemia, CVD, and kidney disease. Therefore, it may be utilized as an alternative to traditional medications or in combination with them to minimize their negative effects as much as possible (Nutmakul et al., 2022).

#### **Anti-cancer** activity

The global cancer burden is growing due to population ageing and growth, as well as changes to people's exposure to risk factors. Various chemical families and bioactive substances from plants demonstrate promising anticancer effects. Numerous studies show Qct's anti-proliferative activity against various cancers, along with its mechanisms of action, including modulation of cellular signalling, binding to cellular receptors and proteins, and inhibition of carcinogen-activating enzymes (Rauf et al., 2018; Madhu et al., 2023).

Langner et al. demonstrated the effects of naturally occurring phytochemical combinations in reducing colon cancer cell growth without adverse effects on healthy colon epithelial cells, suggesting their potential for the prevention and treatment of colon cancer (Langner et al., 2019). Qct-2,3-dioxygenase, present in *Bacillus* spp., is essential for Qct metabolism. Its metabolic products, 2,4,6-trihydroxybenzoic acid (2,4,6-THBA) and 3,4-dihydroxybenzoic acid (3,4-DHBA), possess antiproliferative properties in cancer cells (Sankaranarayanan et al., 2021).

Natural dietary components, such as Qct, are gaining popularity in cancer prevention and therapy. Qct's pro-oxidant properties control tumor growth and trigger apoptotic pathways or cell cycle arrest (Ezzati et al., 2020). With its catechol and OH groups, Qct scavenges free radicals and shows potential for combination therapy with chemoprotective medications. Qct emerges as a potential option for ovarian cancer treatment (Shafabakhsh et al., 2019).

#### **Anti-bacterial activity**

Qct exhibits potent bacteriostatic action against a wide range of bacteria, particularly Grampositive species (Wang et al., 2018). Qct derivatives, including Qct 4',5-diphosphate (QDP), Qct 3',4',3,5,7-pentaphosphate (QPP), and Qct 5'-sulfonic acid (QSA), show high biocompatibility and potency as antibacterial agents, with 100% inhibition of *Listeria monocytogenes*, *Aeromonas hydrophila*, and *Pseudomonas aeruginosa* reported (Osonga et al., 2019).

## **Antifungal activity**

Qct exhibits inhibitory effects against various pathogenic fungi, inducing oxidative stress and altering fungal cell membrane composition, leading to cell death. It shows synergistic effects when combined with other antifungal agents. Rocha et al. (2019) demonstrated a significant reduction in biomass and metabolic activity of Candida strains when using kaempferol and Qct in combination.

## **Anti-tuberculosis activity:**

Lipids present on the cell wall of *Mycobacterium tuberculosis* are responsible for its intracellular survival and pathogenicity. The enzyme pantothenate synthetase (PS or PanC) produces pantothenate (vitamin B5), which is necessary for the biosynthesis of coenzyme A (CoA), an essential element for fatty acid production. Novel anti-TB drug discovery aims to block cell wall synthesis; the fatty acid synthesis of *M. tuberculosis* is greatly affected if PS or PanC is inhibited (Premalatha et al., 2020). The growth-inhibitory properties of Qct against M. *tuberculosis* H37Rv are now well established. Qct's ability to combat *tuberculosis* (TB) suggests its suitability as a prototype for future anti-TB drug delivery methods. Additionally, patients with destructive pulmonary *tuberculosis* (DPTB) who receive chemotherapy in combination with Qct-fixed polyvinylpyrrolidone (PVP) have shown an improved prognosis. Qct has been found to have antioxidant activity, act as a capillary stabilizer, and may also have immunomodulatory effects (Chaudhari et al., 2021).

Besides its role in the tricarboxylic acid (TCA) cycle functionality and cyclic cell development of M. *tuberculosis*, isocitrate lyase, an enzyme, is also required for attachment to host cells. Qct has been shown to improve the repressive effect on *M. tuberculosis* metabolism by reducing *M. tuberculosis* isocitrate lyase (Maiolini et al., 2020).

## Covid-19

Qct can lower blood cholesterol levels in macrophages by altering the expression of ABCA1, a key regulator of reverse cholesterol transport. During the initial stages of atherosclerosis, Qct controls dysregulated cholesterol metabolism and persistent inflammation, resulting in a reduction in the production of foam cells (Pawar et al., 2021). Angiotensin-converting enzyme II (ACE2), required for SARS-CoV-2 entry into cells, has been identified as a human SARS-CoV-2 receptor, offering insights into developing new drugs to combat COVID-19. Qct can attach to the S-receptor-binding protein's domain (RBD), blocking receptors and rendering the SARS-CoV-2 virus ineffective (Roychoudhury et al., 2021; Mbikay et al., 2022). Network pharmacology and bioinformatics analysis support Qct's potential role in host immunomodulation, making it a candidate for COVID-19 treatment (Pan et al., 2020).

#### **Toxic side effects of Qct**

Although the ames test showed Qct as a mutagenic agent, most in vivo animal studies have indicated that Qct is safe, with no carcinogenic effects. In 1999, the International Agency for Research on Cancer (IARC) recommended that Qct should not be classified as a human carcinogen (Utesch et al., 2008; Okamoto, 2005). In vitro studies have suggested that Qct may have a mild negative impact on fetal growth, requiring protective measures, but there is no evidence of teratogenic activity on embryonic growth (Pérez-Pastén et al., 2010). In vivo, experiments also indicated a slight increase in the frequency of malignant tumors in the young offspring of mice lacking DNA repair mechanisms (Vanhees et al., 2011). However, experiments conducted on laboratory rats found that Qct administration significantly increased the liver-to-kidney weight ratio in rats given doses exceeding 314 mg and 157 mg of Qct per kilogram of body weight per day, respectively. Additionally, doses higher than 157 mg Qct/kg body weight/day exhibited pro-oxidant effects (Batiha et al., 2020). Clinical trials in humans have confirmed its tolerance and suitability for use. It is noteworthy that prolonged administration of Qct for several months did not induce any adverse effects on serum electrolytes, kidney and liver function, blood parameters, or hematology. Studies have cautioned against co-administering Qct with digoxin in patients, as it may lead to toxicity (Wang et al., 2004). When orally ingested, dietary Qct undergoes first-pass metabolism in the intestine and liver, resulting in almost complete metabolization, thus minimizing the potential for toxicity. However, the use of high-dose intravenous (IV). Qct in patients with compromised health has been associated with nephrotoxicity (Russo et al., 2012).

#### Conclusion

Quercetin, a natural bioactive compound found in foods like apples, onions, and berries, is gaining attention for its medicinal potential. It shows promise in treating ailments such as diabetes, heart disease, and osteoporosis. Consumption of flavonoids like quercetin is linked to a reduced risk of cardiovascular disease. Its antioxidant, anti-inflammatory, and anti-tumor properties suggest potential clinical applications. Quercetin also exhibits antibacterial activity, though this aspect requires further investigation. Nevertheless, its broad-spectrum antibacterial nature could offer alternatives to antibiotics for treating infectious bacterial diseases. Further research is required to explore its biological as well as therapeutic applications.

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